AMENDMENTS TO THE CLAIMS

Claim 1 (amended). A compound that binds allosterically to MMP-13 and that comprises first and second hydrophobic groups and first and second hydrogen bond acceptors, wherein:

(a) the relative positions of centroids of the above features are defined by the following Cartesian coordinates in Å:

(i) first hydrogen bond acceptor, 0.00, 0.00, 0.00;

(ii) second hydrogen bond acceptor, 5.08, 2.23, 0.00;

(iii) first hydrophobic group, –1.52, -3.06, -0.23;

(iv) second hydrophobic group, 9.07, 0.00, 0.00; and

(b) tolerances in the positions of the hydrophobic groups and the hydrogen bond acceptors are ± 1.0 Å and ± 1.5 Å respectively, wherein the compound is a substituted 2,4-dioxo-pyrido[3,4-d]pyrimidine.

Claim 2 (original). The compound of claim 1, wherein the first hydrophobic group contains a bicyclic ring system containing between 8 and 10 atoms and which may contain one or several heteroatoms, or a 5- or 6-membered monocyclic aromatic group which may contain one or more heteroatoms and which may be 4-substituted or 3,4-disubstituted, but which is of width (including substituents) less than 4.0 Å.

Claim 3 (original). The compound of claim 2, wherein the pi-system of the aromatic ring is electron rich.

Claim 4 (original). The compound of claim 1, wherein first hydrophobic group, is linked by a first linker chain which is three atoms long to a first 5- or 6-membered ring of the scaffold, the first linker chain atom adjacent to said first scaffold ring forming part of the first hydrogen bond acceptor.

Claim 5 (original). The compound of claim 4, wherein the first linker chain has a methylene group located adjacent to the hydrophobic group.

Claim 6 (original). The compound of claim 4, wherein the scaffold further comprises a second scaffold ring fused to the first scaffold ring at locations two and three ring atoms distant from the junction between the first scaffold ring and the first linker chain, and the atom of the second scaffold ring adjacent to the atom of the first scaffold ring that is two positions distant from said junction forms part of the second hydrogen bond acceptor.

Claim 7 (original). The compound of claim 6, wherein the atom of the second scaffold ring adjacent to the atom of the first scaffold ring that is three positions distant from said junction has a substituent which is a single atom or is a methyl group.

Claim 8 (original). The compound of claim 1, wherein the second hydrophobic group is a 5- or 6-membered aromatic ring which may contain one or several heteroatoms, a bicyclic ring system containing between 8 and 10 atoms and which may contain one or several heteroatoms, or a planar saturated or unsaturated system.

Claim 9 (amended). A compound that binds allosterically to MMP-13 and that comprises a hydrophobic group and first, second and third hydrogen bond acceptors, wherein:

(a) the relative positions of centroids of the above features are defined by the following Cartesian coordinates in Å:

(i) first hydrogen bond acceptor, 0.00, 0.00, 0.00;

(ii) second hydrogen bond acceptor, 5.08, 2.23 ,0.0;

(iii) third hydrogen bond acceptor, 7.15, 0.80, 0.00;

(iv) first hydrophobic group, –1.52,-3.06, -0.23; and

(b) tolerances in the positions of the hydrophobic group and the hydrogen bond acceptors are ± 1.0 Å and ± 1.5 Å respectively, wherein the compound is a substituted 2,4-dioxo-pyrido[3,4-d]pyrimidine.

Claim 10 (original). The compound claim 9, wherein the first hydrophobic group contains a bicyclic ring system containing between 8 and 10 atoms and which may contain one or several heteroatoms, or a 5- or 6-membered monocyclic aromatic group which may contain one or more heteroatoms and which may be 4-substituted or 3,4-disubstituted, but which is of width (including substituents) less than 4.0 Å.

Claim 11 (original). The compound of claim 10, wherein the pi-system of the aromatic ring is electron rich.

Claim 12 (original). The compound of claim 10, wherein first hydrophobic group, is linked by a first linker chain which is three atoms long to a first 5- or 6-membered ring of the scaffold, the first linker chain atom adjacent to said first scaffold ring forming part of the first hydrogen bond acceptor.

Claim 13 (original). The compound of claim 12, wherein the chain has a methylene group located adjacent to the hydrophobic group.

Claim 14 (original). The compound of claim 12, wherein the scaffold further comprises a second ring fused to the first scaffold ring at locations two and three ring atoms distant from the junction between the first scaffold ring and the chain, and the atom of the second scaffold ring adjacent to the atom of the first scaffold ring that is two positions distant from said junction forms part of the second hydrogen bond acceptor.

Claim 15 (original). The compound of claim 14, wherein the atom of the second scaffold ring adjacent to the atom of the first scaffold ring that is three positions distant from said junction has a substituent which is a single atom or is a methyl group.

Claim 16 (original). The compound of claim 14, wherein the second scaffold ring is 6-membered and the atom of the second scaffold ring that is two positions distant from the atom that forms part of the second hydrogen bond acceptor forms part of the third hydrogen bond acceptor.

Claim 17 (original). The compound of claim 14, wherein the second scaffold ring is 6-membered and a third scaffold ring is fused to the second scaffold ring at those atoms of the second scaffold ring which are two and three positions distant from the atom that forms part of the second hydrogen bond acceptor, an atom of the third scaffold ring forming part of the third hydrogen bond acceptor.

Claim 18 (amended). A compound that binds allosterically to MMP-13 and that comprises first and second hydrophobic groups and first, second and third hydrogen bond acceptors, wherein:

(a) the relative positions of centroids of the above features are defined by the following Cartesian coordinates in Å:

(i) first hydrogen bond acceptor, 0.00, 0.00, 0.00;

(ii) second hydrogen bond acceptor, 5.08, 2.23 ,0.0;

(iii) third hydrogen bond acceptor, 7.15, 0.80, 0.00;

(iv) first hydrophobic group, –1.52,-3.06, -0.23;

(v) second hydrophobic group, 9.07, 0.00, 0.00; and

(b) tolerances in the positions of the hydrophobic groups and the hydrogen bond acceptors are ± 1.0 Å and ± 1.5 Å respectively, wherein the compound is a substituted 2,4-dioxo-pyrido[3,4-d]pyrimidine.

Claim 19 (original). The compound of claim 18, wherein the first hydrophobic group contains a bicyclic ring system containing between 8 and 10 atoms and which may contain one or several heteroatoms, or a 5- or 6-membered monocyclic aromatic group which may contain one or more heteroatoms and which may be 4-substituted or 3,4-disubstituted, but which is of width (including substituents) less than 4.0 Å.

Claim 20 (original). The compound of claim 19, wherein the pi-system of the aromatic ring is electron rich.

Claim 21 (original). The compound of claim 19, wherein first hydrophobic group, is linked by a first linker chain which is three atoms long to a first 5- or 6-membered ring of the scaffold, the first linker chain atom adjacent to said first scaffold ring forming part of the first hydrogen bond acceptor.

Claim 22 (original). The compound of claim 21, wherein the chain has a methylene group located adjacent to the hydrophobic group.

Claim 23 (original). The compound of claim 21, wherein the scaffold further comprises a second scaffold ring fused to the first scaffold ring at locations two and three ring atoms distant from the junction between the first scaffold ring and the first linker chain, and the atom of the second scaffold ring adjacent to the atom of the first scaffold ring that is two positions distant from said junction forms part of the second hydrogen bond acceptor.

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Claim 24 (original). The compound of claim 23, wherein the atom of the second scaffold ring adjacent to the atom of the first scaffold ring that is three positions distant from said junction has a substituent which is a single atom or is a methyl group.

Claim 25 (original). The compound of claim 23, wherein the second scaffold ring is 6-membered and the atom of the second scaffold ring that is two positions distant from the atom that forms part of the second hydrogen bond acceptor forms part of the third hydrogen bond acceptor.

Claim 26 (original). The compound of claim 23, wherein the second scaffold ring is 6-membered and a third scaffold ring is fused to the second scaffold ring at those atoms of the second scaffold ring which are two and three positions distant from the atom that forms part of the second hydrogen bond acceptor, an atom of the third scaffold ring forming part of the third hydrogen bond acceptor.

Claim 27 (original). The compound of claim 18, wherein the second hydrophobic group is a 5- or 6-membered aromatic ring which may contain one or several heteroatoms, a bicyclic ring system containing between 8 and 10 atoms and which may contain one or several heteroatoms, or a planar saturated or unsaturated system.

Claim 28 (amended). A ligand that binds allosterically to MMP-13 and that comprises a scaffold, first and second hydrogen bond acceptors and first and second hydrophobic groups connected by side chains to the scaffold, a cyclic structure forming part of the scaffold being located between the first and second hydrogen bond acceptors, and the hydrogen bond acceptors and hydrophobic groups being arranged so that when the ligand binds to MMP-13:

the first and second hydrogen bond acceptors bond respectively with Thr245, Thr 247;

B1 the first hydrophobic group locates within the S1' channel; and

the second hydrophobic group is relatively open to solvent, wherein the ligand is a substituted 2,4-dioxo-pyrido[3,4-d]pyrimidine.

Claim 29 (amended). A ligand that binds allosterically to MMP-13 and that comprises a scaffold, first, second and third hydrogen bond acceptors, and a hydrophobic group connected by a side chain to the scaffold, a cyclic structure forming part of the scaffold being located between the first and second hydrogen bond acceptors, and the hydrogen bond acceptors and hydrophobic group being arranged so that when the ligand binds to MMP-13:

the first, second and third hydrogen bond acceptors bond respectively with Thr245, Thr 247 and Met 253; and

the first hydrophobic group locates within the S1' channel, wherein the ligand is a substituted 2,4-dioxo-pyrido[3,4-d]pyrimidine.

Claim 30 (amended). A ligand that binds allosterically to MMP-13 and that comprises a scaffold, first, second and third hydrogen bond acceptors, and first and second hydrophobic groups connected by side chains to the scaffold, a cyclic structure

forming part of the scaffold being located between the first and second hydrogen bond acceptors, and the hydrogen bond acceptors and hydrophobic groups being arranged so that when the ligand binds to MMP-13:

the first, second and third hydrogen bond acceptors bond respectively with Thr245, Thr 247 and Met 253;

the first hydrophobic group locates within the S1' channel; and

the second hydrophobic group is open to solvent, wherein the ligand is a substituted 2,4-dioxo-pyrido[3,4-d]pyrimidine.

Claim 31 (amended). A ligand that binds allosterically to the S1' and S1" pockets of MMP 13, wherein the ligand is a substituted 2,4-dioxo-pyrido[3,4-d]pyrimidine.

Claim 32 (original). The ligand of claim 31, wherein the S1" pocket is defined by amino acid residues from Tyr246 to Pro255.

Claim 33 (original). A pharmaceutical composition comprising a compound as claimed in claim 1 claim and a pharmaceutically acceptable excipient.

Claim 34 (original). A pharmaceutical composition comprising a compound as claimed in claim 9 and a pharmaceutically acceptable excipient.

Claim 35 (original). A pharmaceutical composition comprising a compound as claimed in claim 18 and a pharmaceutically acceptable excipient.

Claims 36-45 (canceled).